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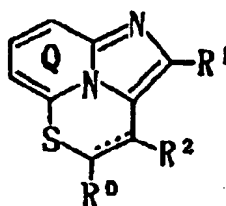


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(54) Title: FUSED IMIDAZOPYRIDINE DERIVATIVES AS ANTIHYPERLIPIDEMIC AGENTS



(I)

(57) Abstract

A novel compound of formula (I) wherein ring Q is an optionally substituted pyridine ring; one of R⁰, R¹ and R² is -Y⁰-Z⁰, and the other two groups are a hydrogen, a halogen, an optionally substituted hydroxy group, a hydrocarbon group that may be an optionally substituted hydrocarbon group or an acyl group; Y⁰ is a bond or an optionally substituted bivalent hydrocarbon group; Z⁰ is a basic group which may be bonded via oxygen, nitrogen, -CO-, -CS-, -SO₂N(R³)- (where R³ is hydrogen or an optionally substituted hydrocarbon group), or S(O)_n (wherein n is to 0, 1 or 2); is a single bond or a double bond, or a salt thereof, which has an excellent LDL receptor up-regulating, blood-lipids lowering, blood-sugar lowering and diabetic complication-ameliorating activity.

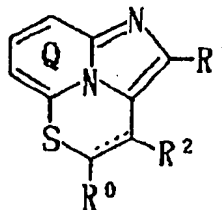
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CLAIMS

1. A compound of the formula:



wherein ring Q is an optionally substituted pyridine ring;

one of R^0 , R^1 and R^2 is $-Y^0-Z^0$, and the other two groups are a hydrogen, a halogen, an optionally substituted hydroxy group, an optionally substituted hydrocarbon group or an acyl group;

Y^0 is a bond or an optionally substituted divalent hydrocarbon group;

Z^0 is a basic group which may be bonded via oxygen, nitrogen, $-CO-$, $-CS-$, $-SO_2N(R^3)-$ (wherein R^3 is a hydrogen or an optionally substituted hydrocarbon group), or

$-S(O)_n-$ (wherein n is 0, 1 or 2); and

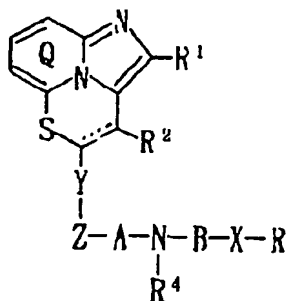
----- is a single bond or a double bond, or a salt thereof.

2. A compound of claim 1, wherein R^0 is $-Y^0-Z^0$, wherein Y^0 and Z^0 are of the same meanings as defined in claim 1.

3. A compound of claim 1, wherein Z^0 is a group with a molecular weight of not greater than 1000.

4. A compound of claim 1 which is a compound of the formula:


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wherein ring Q is an optionally substituted pyridine ring;

A and B independently are an optionally substituted divalent hydrocarbon group which may be bonded via $-\text{CON}(\text{R}^{4a})-$, $-\text{CO}-$ or $-\text{N}(\text{R}^{4a})-$;

X is a bond, oxygen, sulfur, $-\text{N}(\text{R}^5)\text{CO}-$, $-\text{CO}(\text{R}^5)-$, $-\text{CO}-$ or $-\text{N}(\text{R}^5)-$;

Y is a bond, $-\text{CH}=\text{CH}-$ or $-\text{CH}=\text{CH}-$  ;

Z is $-\text{CO}-$, $-\text{COO}-$, $-\text{CON}(\text{R}^3)-$, $-\text{SO}_2\text{N}(\text{R}^3)-$ or $-\text{S}(\text{O})_m-$ (wherein m is 0, 1 or 2);

R^1 and R^2 independently are a hydrogen, a halogen, an optionally substituted hydroxy group, an optionally substituted hydrocarbon group or an acyl group;

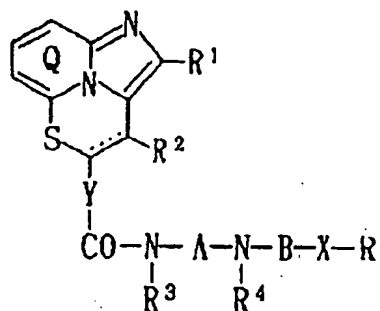
R^3 , R^4 , R^{4a} and R^5 independently are a hydrogen or an optionally substituted hydrocarbon group; or

R^3 and A, R^4 and A, R^4 and B, R^4 and R^5 , or R^4 and R may independently be bonded to each other to form a ring;

R is an optionally substituted hydrocarbon group or an optionally substituted heterocyclic group; and

----- is a single bond or a double bond, or a salt thereof.

5. A compound of claim 1 which is a compound of the formula:



wherein ring Q is an optionally substituted pyridine ring;

A and B independently are an optionally substituted divalent hydrocarbon group which may be bonded via $-\text{CON}(\text{R}^{4a})-$, $-\text{CO}-$ or $-\text{N}(\text{R}^{4a})-$;

X is a bond, oxygen, sulfur, $-\text{N}(\text{R}^5)\text{CO}-$, $-\text{CO}(\text{R}^5)-$, $-\text{CO}-$ or $-\text{N}(\text{R}^5)-$;

Y is a bond, $-\text{CH}=\text{CH}-$ or $-\text{CH}=\text{CH}-$;

Z is $-\text{CO}-$, $-\text{COO}-$, $-\text{CON}(\text{R}^3)-$, $-\text{SO}_2\text{N}(\text{R}^3)-$ or $-\text{S}(\text{O})\text{m}-$ (wherein m is 0, 1 or 2);

R^1 and R^2 independently are a hydrogen, a halogen, an optionally substituted hydroxy group, an optionally substituted hydrocarbon group or an acyl group;

R^3 , R^4 , R^{4a} and R^5 independently are a hydrogen or an optionally substituted hydrocarbon group; or



R^3 and A, R^4 and A, R^4 and B, R^4 and R^5 , or R^4 and R independently may be bonded to each other to form a ring;

R is an optionally substituted hydrocarbon group or an optionally substituted heterocyclic group; and

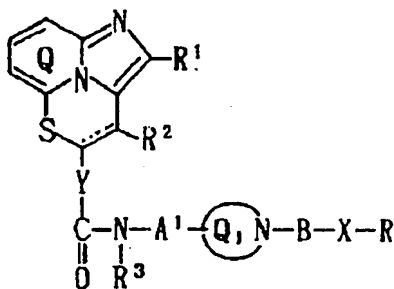
----- is a single bond or a double bond, or a salt thereof.

6. A compound of claim 5, wherein A and B independently are an alkylene group; X is a bond; and

R^3 and R^4 independently are a hydrogen or an optionally substituted alkyl, cycloalkyl, alkenyl, aralkyl or aryl group.

7. A compound of claim 5, wherein ring Q is an unsubstituted pyridine ring; X is a bond; Y is a bond,  OR ; A and B independently are a C_{1-15} alkylene group; R^1 and R^2 independently are a hydrogen; R^3 and R^4 independently are a hydrogen or a C_{1-15} alkyl, C_{3-8} cycloalkyl, C_{2-18} alkenyl, C_{7-16} aralkyl or C_{6-14} aryl group; and R is a C_{6-14} aryl group.

8. A compound of claim 1 which is a compound of the formula:




wherein ring Q is an optionally substituted pyridine ring;

ring Q_1 is an optionally substituted nitrogen-containing heterocyclic ring;

A^1 is a bond or an optionally substituted divalent hydrocarbon group which may be bonded via $-\text{CON}(R^{4a})-$, $-\text{CO}-$ or $-\text{N}(R^{4a})-$;

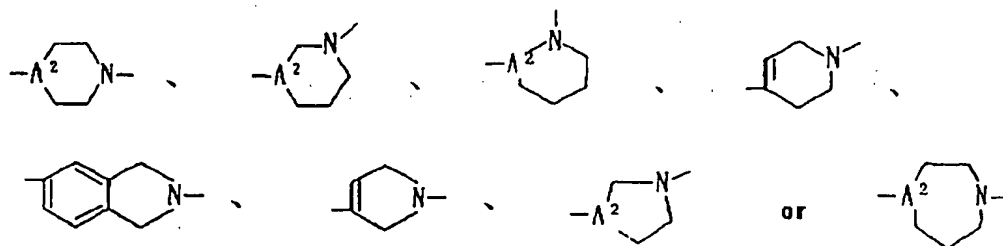
B is an optionally substituted divalent hydrocarbon group;

X is a bond, oxygen, sulfur, $-\text{N}(R^5)\text{CO}-$, $-\text{CO}(R^5)-$, $-\text{CO}-$ or $-\text{N}(R^5)-$;

Y is a bond, $-\text{CH}=\text{CH}-$ or $-\text{CH}=\text{CH}-$  ;

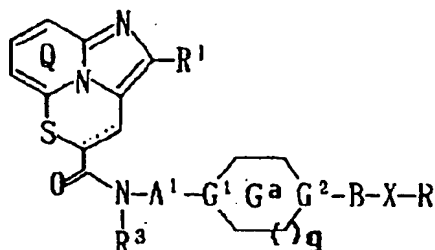
R^1 and R^2 independently are a hydrogen, a halogen, an optionally substituted hydroxy group, an optionally substituted hydrocarbon group or an acyl group;
 R^3 , R^{4a} and R^5 independently are a hydrogen or an optionally substituted hydrocarbon group; or
 R^3 and A^1 may be bonded to each other to form a ring;
 R is an optionally substituted hydrocarbon group or an optionally substituted heterocyclic group; and
 ===== is a single bond or a double bond, or a salt thereof.

9. A compound of claim 8, wherein ring Q is an unsubstituted pyridine ring; R^1 and R^2 are a hydrogen; R^3 is a hydrogen or a C_{1-15} alkyl, C_{3-8} cycloalkyl, C_{2-18} alkenyl, C_{7-16} aralkyl or C_{6-14} aryl group; A^1 is (i) a bond, (ii) a C_{1-15} alkylene group which may be substituted by 1 to 3 substituents selected from the group consisting of hydroxy, oxo and phenyl, (iii) a C_{2-16} alkenylene group or (iv) a phenylene group; B is (i) a C_{1-15} alkylene group which may be substituted by 1 to 3 substituents selected from the group consisting of hydroxy, oxo and phenyl, (ii) a C_{2-16} alkenylene group or (iii) a phenylene group; ring Q_1 is a group of the formula:



wherein A^2 is $=\text{C}$ or CH ; X is a bond, oxygen, sulfur or $-\text{CON}(\text{R}^5)-$; R^5 is a hydrogen or a C_{1-15} alkyl group.

10. A compound of claim 1 which is a compound of the formula:



wherein ring Q is an optionally substituted pyridine ring;

A¹ is a bond or an optionally substituted divalent hydrocarbon group which may be bonded via -CON(R^{4a})-, -CO- or -N(R^{4a})-;

B is an optionally substituted divalent hydrocarbon group;

X is a bond, oxygen, sulfur, -N(R⁵)CO-, -CON(R⁵)-, -CO- or -N(R⁵)-;

R¹ is a hydrogen, a halogen, an optionally substituted hydroxy group, an optionally substituted hydrocarbon group or an acyl group;

R³, R^{4a} and R⁵ independently are a hydrogen or an optionally substituted hydrocarbon group;

R is an optionally substituted hydrocarbon group or an optionally substituted heterocyclic group;

one of G¹ and G² is N, and the other is CH or N;

ring G^a is an optionally substituted ring;

g is 0, 1 or 2; and

----- is a single bond or a double bond, or a salt thereof.

11. A compound of claim 10, wherein ring Q is a pyridine ring which may be substituted by 1 to 3 substituents selected from the group consisting of nitro, hydroxy, cyano, carbamoyl, mono- or di-C₁₋₄

alkyl-carbamoyl, carboxy, C₁₋₄ alkoxy-carbonyl, sulfo, halogen, C₁₋₄ alkoxy, phenoxy, naphthoxy, benzyloxy, halophenoxy, C₁₋₄ alkylthio, mercapto, phenylthio, pyridylthio, C₁₋₄ alkylsulfinyl, phenylsulfinyl, C₁₋₄ alkylsulfonyl, phenylsulfonyl, amino, C₁₋₃ acylamino, mono- or di-C₁₋₄ alkylamino, C₁₋₄ alkyl and C₁₋₄ haloalkyl.

12. A compound of claim 10, A¹ is a bond or a C₁₋₁₅ alkylene, C₂₋₁₆ alkenylene group which may be bonded via -CON(R^{4a})-, -CO- or -N(R^{4a})-, wherein R^{4a} is of the same meaning as defined in claim 10.

13. A compound of claim 10, B is a C₁₋₁₅ alkylene or C₂₋₁₆ alkenylene group.

14. A compound of claim 10, X is a bond, oxygen, sulfur, -CONH- or -CO-.

15. A compound of claim 10, R¹ is (1) a hydrogen, (2) a halogen, (3) a hydroxy group which may be substituted by a C₁₋₆ alkyl, phenyl, C₇₋₁₀ aralkyl, formyl, C₁₋₆ alkyl-carbonyl, phenyloxycarbonyl, C₇₋₁₀ aralkyloxy-carbonyl, pyranyl, furanyl or silyl group, (4) a C₁₋₁₅ alkyl, C₃₋₈ cycloalkyl, C₂₋₁₈ alkenyl, C₇₋₁₆ aralkyl or C₆₋₁₄ aryl group or (5) a C₁₋₆ alkoxy-carbonyl, mono-C₁₋₆ alkyl-carbamoyl, di-C₁₋₆ alkyl-carbamoyl or C₁₋₁₀ alkanoyl group.

16. A compound of claim 10, R³ is a hydrogen or a C₁₋₁₅ alkyl, C₃₋₈ cycloalkyl, C₂₋₁₈ alkenyl, C₇₋₁₆ aralkyl or C₆₋₁₄ aryl group.

17. A compound of claim 10, R is (1) a C₁₋₁₅ alkyl, C₃₋₈

cycloalkyl or C₂₋₁₈ alkenyl group which may be substituted by 1 to 5 substituents selected from the group consisting of (i) nitro, (ii) hydroxy, (iii) cyano, (iv) carbamoyl, (v) mono- or di-C₁₋₄ alkyl-carbamoyl, (vi) carboxy, (vii) C₁₋₄ alkoxy-carbonyl, (viii) sulfo, (ix) halogen, (x) C₁₋₄ alkoxy, (xi) phenoxy, (xii) halophenoxy, (xiii) C₁₋₄ alkylthio, (xiv) mercapto, (xv) phenylthio, (xvi) pyridylthio, (xvii) C₁₋₄ alkylsulfinyl, (xviii) C₁₋₄ alkylsulfonyl, (xix) amino, (xx) C₁₋₃ alkanoylamino, (xxi) mono- or di-C₁₋₄ alkylamino, (xxii) 4- to 6-membered cyclic amino, (xxiii) C₁₋₃ alkanoyl, (xxiv) benzoyl and (xxv) 5- to 10-membered heterocyclic group;

(2) a C₇₋₁₆ aralkyl group which may be substituted by 1 to 4 substituents selected from the group consisting of (i) halogen, (ii) C₁₋₄ alkyl, (iii) C₂₋₆ alkenyl, (iv) C₁₋₃ alkanoyl, (v) C₁₋₄ alkoxy, (vi) nitro, (vii) cyano, (viii) hydroxy, (ix) C₁₋₄ alkoxy-carbonyl, (x) carbamoyl, (xi) mono- or di-C₁₋₄ alkyl-carbamoyl and (xii) mono- or di-C₂₋₄ alkenyl-carbamoyl;

(3) a C₆₋₁₄ aryl group which may be substituted by 1 to 4 substituents selected from the group consisting of (i) halogen, (ii) C₁₋₄ alkyl, (iii) C₁₋₄ haloalkyl, (iv) C₁₋₄ haloalkoxy, (v) C₁₋₄ alkoxy, (vi) C₁₋₄ alkylthio, (vii) hydroxy, (viii) carboxy, (ix) cyano, (x) nitro, (xi) amino, (xii) mono- or di-C₁₋₄ alkylamino, (xiii) formyl, (xiv) mercapto, (xv) C₁₋₄ alkyl-carbonyl, (xvi) C₁₋₄ alkoxy-carbonyl, (xvii) sulfo, (xviii) C₁₋₄ alkylsulfonyl, (xix) carbamoyl, (xx) mono- or di-C₁₋₄ alkyl-carbamoyl, (xxi) oxo and (xxii) thioxo; or

(4) a 5- or 6-membered monocyclic heterocyclic group containing 1 to 4 hetero-atoms selected from oxygen, sulfur and nitrogen or a fused bicyclic heterocyclic group containing 1 to 6 hetero-atoms selected from oxygen, sulfur and nitrogen, each of which may be

substituted by 1 to 4 substituents selected from the group consisting of (i) halogen, (ii) C₁₋₄ alkyl, (iii) C₁₋₄ haloalkyl, (iv) C₁₋₄ haloalkoxy, (v) C₁₋₄ alkoxy, (vi) C₁₋₄ alkylthio, (vii) hydroxy, (viii) carboxy, (ix) cyano, (x) nitro, (xi) amino, (xii) mono- or di-C₁₋₄ alkylamino, (xiii) formyl, (xiv) mercapto, (xv) C₁₋₄ alkyl-carbonyl, (xvi) C₁₋₄ alkoxy-carbonyl, (xvii) sulfo, (xviii) C₁₋₄ alkylsulfonyl, (xix) carbamoyl, (xx) mono- or di-C₁₋₄ alkyl-carbamoyl, (xxi) oxo and (xxii) thioxo.

18. A compound of claim 10, wherein ring G^a is a ring which may be substituted by 1 or 2 substituents selected from the group consisting of oxo and C₁₋₆ alkyl.

19. A compound of claim 10, wherein ring Q is an unsubstituted pyridine ring; R¹ and R³ are a hydrogen; G¹ is CH; G² is N; g is 1; and R is an optionally substituted hydrocarbon group or an optionally substituted heterocyclic group.

20. A compound of claim 19, wherein ring G^a is unsubstituted ring.

21. A compound of claim 19, wherein A¹ is a bond or a C₁₋₆ alkylene group.

22. A compound of claim 19, wherein A¹ is a bond.

23. A compound of claim 19, wherein B is a C₁₋₆ alkylene group.

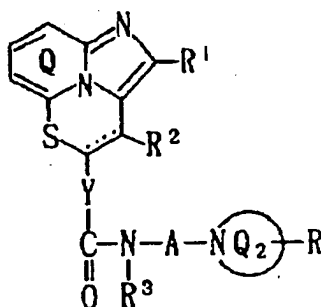
24. A compound of claim 19, X is a bond.

25. A compound of claim 10, ring Q is an unsubstituted pyridine ring; R^1 and R^2 are a hydrogen; A^1 is a bond; G^1 is CH; G^2 is N; ring G^3 is a ring which may be substituted by 1 or 2 substituents selected from the group consisting of oxo and C_{1-6} alkyl; g is 1; B is a C_{1-6} alkylene group; X is a bond; and R is an optionally substituted phenyl group.

26. A compound of claim 25, ring G^3 is unsubstituted ring.

27. A compound of claim 25, wherein R is a phenyl group which may be substituted by 1 to 3 substituents selected from the group consisting of halogen, hydroxy, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy and C_{1-4} haloalkoxy.


28. A compound of claim 1 which is a compound of the formula:



wherein ring Q is an optionally substituted pyridine ring;

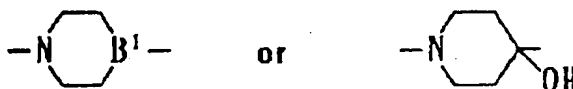
ring Q_2 is an optionally substituted nitrogen-containing heterocyclic ring;

A is an optionally substituted divalent hydrocarbon group which may be bounded via $-\text{CON}(R^{4a})-$, $-\text{CO}-$ or $-\text{N}(R^{4a})-$;

Y is a bond, $-\text{CH}=\text{CH}-$ or $-\text{CH}=\text{CH}-$  ;

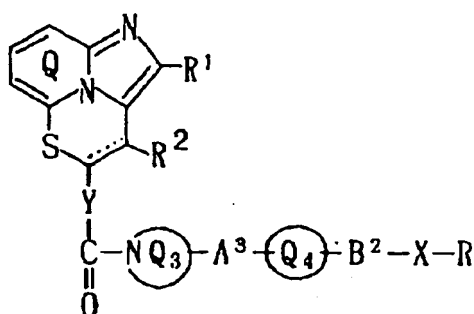
R^1 and R^2 independently are a hydrogen, a halogen, an optionally substituted hydroxy group, an optionally substituted hydrocarbon group or an acyl group;
 R^3 and R^{4a} independently are a hydrogen or an optionally substituted hydrocarbon group; or
 R^3 and A may be bonded to each other to form a ring;
 R is an optionally substituted hydrocarbon group or an optionally substituted heterocyclic group; and
 ----- is a single bond or a double bond, or a salt thereof.

29. A compound of claim 28, wherein ring Q is an unsubstituted pyridine ring; R^1 and R^2 are a hydrogen; R^3 is a hydrogen or a C_{1-15} alkyl, C_{3-8} cycloalkyl, C_{2-18} alkenyl, C_{7-16} aralkyl or C_{6-14} aryl group; A is (i) a C_{1-15} alkylene group which may be substituted by 1 to 3 substituents selected from the group consisting of hydroxy, oxo and phenyl, (ii) a C_{2-16} alkenylene group or (iii) a phenylene group; ring Q_2 is a group of the formula:



wherein B^1 is $=\text{C}$, CH or N.


30. A compound of claim 1 which is a compound of the formula:



wherein ring Q is an optionally substituted pyridine ring;

ring Q₃ and Q₄ independently are an optionally substituted nitrogen-containing heterocyclic ring; A³ and B² independently are a bond or an optionally substituted divalent hydrocarbon group;

X is a bond, oxygen, sulfur, -N(R⁵)CO-, -CON(R⁵)-, -CO- or -N(R⁵)-;

Y is a bond, -CH=CH- or -CH=CH-  ;

R¹ and R² independently are a hydrogen, a halogen, an optionally substituted hydroxy group, an optionally substituted hydrocarbon group or an acyl group;

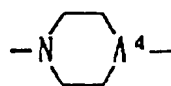
R⁵ is a hydrogen or an optionally substituted hydrocarbon group;

R is an optionally substituted hydrocarbon group or an optionally substituted heterocyclic group; and

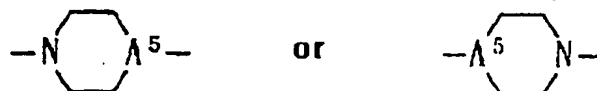
----- is a single bond or a double bond, or a salt thereof.

31. A compound of claim 30, wherein ring Q is an unsubstituted pyridine ring; R¹ and R² are a hydrogen; A³ and B² independently are a bond or a C₁₋₁₅ alkylene, C₂₋₁₆ alkenylene or phenylene group; ring Q₃ is a group of the formula:

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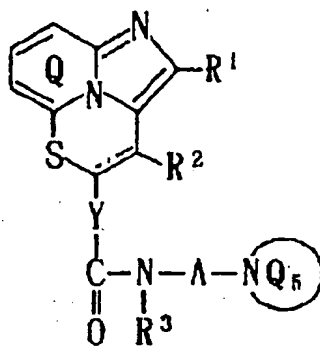


wherein A^4 is =C or CH; ring Q_4 is a group of the formula:



wherein A^5 is =C or CH.

32. A compound of claim 1 which is a compound of the formula:



wherein ring Q is an optionally substituted pyridine ring;

ring Q_5 is an optionally substituted nitrogen-containing heterocyclic ring;

A is an optionally substituted divalent hydrocarbon group which may be bonded via $-\text{CON}(\text{R}^{4a})-$, $-\text{CO}-$ or $-\text{N}(\text{R}^{4a})-$;

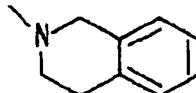
Y is a bond, $-\text{CH}=\text{CH}-$ or $-\text{CH}=\text{CH}-$;

R^1 and R^2 independently are a hydrogen, a halogen, an optionally substituted hydroxy group, an optionally substituted hydrocarbon group or an acyl group;

R^3 and R^{4a} independently are a hydrogen or an optionally substituted hydrocarbon group; and

----- is a single bond or a double bond, or a salt thereof.

33. A compound of claim 32, wherein ring Q is an unsubstituted pyridine ring; R¹ and R² are a hydrogen; R³ is a hydrogen or a C₁₋₁₅ alkyl, C₃₋₈ cycloalkyl, C₂₋₁₈ alkenyl, C₇₋₁₆ aralkyl or C₆₋₁₄ aryl group; A is a C₁₋₁₅ alkylene, C₂₋₁₆ alkenylene or phenylene group; ring Q₅ is a group of the formula:



34. A compound of claim 1 which is (R)-N-[1-(1,4-benzodioxan-2-ylmethyl)piperidin-4-ylmethyl]-5-thia-1,8b-diazaacenaphthylene-4-carboxamide, or a pharmaceutically acceptable salt thereof.

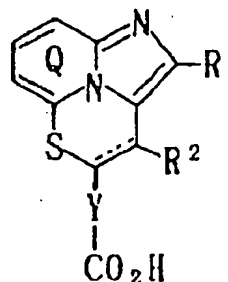
35. A compound of claim 1 which is N-[1-(3-phenylpropyl)piperidin-4-ylmethyl]-3-(5-thia-1,8b-diazaacenaphthylene-4-yl)acrylamide, or a pharmaceutically acceptable salt thereof.

36. A compound of claim 1 which is N-[4-(4-phenylpiperidin-1-yl)butan-1-yl]-5-thia-1,8b-diazaacenaphthylene-4-carboxamide, or a pharmaceutically acceptable salt thereof.

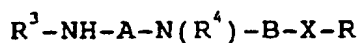
37. A compound of claim 1 which is N-[1-(3-phenylpropan-1-yl)piperidin-4-yl]-5-thia-1,8b-diazaacenaphthylene-4-carboxamide, or a pharmaceutically acceptable salt thereof.

38. A process for producing a compound of claim 5, which comprises condensing a compound of the formula:

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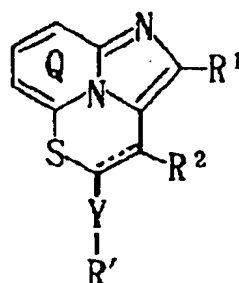


wherein all symbols are of the same meanings as defined in claim 5, or a salt thereof with a compound of the formula:



wherein all symbols are of the same meanings as defined in claim 5, or a salt thereof.

39. A compound of the formula:



wherein R' is an optionally protected COOH, CH₂OH or CHO group; and the other symbols are of the same meanings as defined in claim 4, or a salt thereof.

40. A pharmaceutical composition which comprises a compound of claim 1.

41. A pharmaceutical composition of claim 40, which is an up-regulator of low density lipoprotein receptor.

42. A pharmaceutical composition of claim 40, which is a therapeutic agent for lowering lipids in blood.

43. A pharmaceutical composition of claim 40, which is a therapeutic agent for atherosclerosis.

44. A pharmaceutical composition of claim 40, which is an agent for lowering blood sugar.

45. A pharmaceutical composition of claim 40, which is a therapeutic agent for diabetic complications.

46. Use of a compound of claim 1 for the manufacture of a medicament for lowering lipids in blood.

47. Method for lowering lipids in blood in a mammal which comprises administering to said mammal an effective amount of a compound of claim 1.